Remarks

Overview

In the Office Action under reply, claims 1-26 are pending and have been rejected as follows: (1) the Examiner has maintained the rejection, first made in the Office Action mailed September 10, 2004, of claims 1-26 under 35 U.S.C. § 112; (2) claims 1-26 have been rejected under 35 U.S.C. § 102(a) as being anticipated by Guzaev et al. (US 6,121,437); (3) claims 1-26 have been rejected under 35 U.S.C. § 102(a) as being anticipated by Guzaev et al. (Tetrahedron Letters, vol. 41, 2000, pp. 5623-5626); and (4) claims 1-26 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Seliger et al. (US 5,700,919).

Applicant acknowledges with appreciation the Examiner's removal of the objections from the Office Action mailed September 10, 2004. The abovementioned rejections are overcome in part by the amendment made herein and otherwise traversed for at least the reasons described below.

Amendments to the specification

Paragraphs **[00049], [00059], [00066], [00068]** and **[00073]** have been amended to correct a typographical error in which the β-thiobenzoylethyl group was incorrectly named as -thiobenzoylethyl. This amendment is supported by the specification of Serial No. 09/691,824, now US Patent No. 6,693,187 (see, e.g., line 59 of col. 12 or line 56 of col. 15), the disclosure of which has been incorporated into the current application by reference. No new matter has been added by this amendment.

Amendments to the claims

By the foregoing amendments, claims 1, 2, 15 and 16 have been amended to recite the proviso that "P is directly attached to at least one carbon atom." Support for this amendment follows from the claim language, as well as the specification, which states that the compounds of the invention are "phosphinoamidite carboxylates and analogs thereof" (paragraph **[00064]**, page 22). Claims 1, 2, 15, and 16 have also been amended to recite the limitation that "said substituted moieties refer to molecules wherein one or more atoms of hydrogen have been replaced with a lower hydrocarbyl moiety or functional group selected from hydroxyl, alkoxy, thio, amino, and

halo." Support for this amendment can be found in the specification, for example in paragraph **[00053]** on page 18 (substituents that are functional groups), and paragraph **[00050]** on page 17 (lower hydrocarbyl).

Claims 10 and 22 have been amended to correct a typographical error in which the β-thiobenzoylethyl group was incorrectly named as .-thiobenzoylethyl. This amendment is supported by the specification as amended (see previous section, Amendments to the Specification).

Rejection under 35 U.S.C. §112, second paragraph

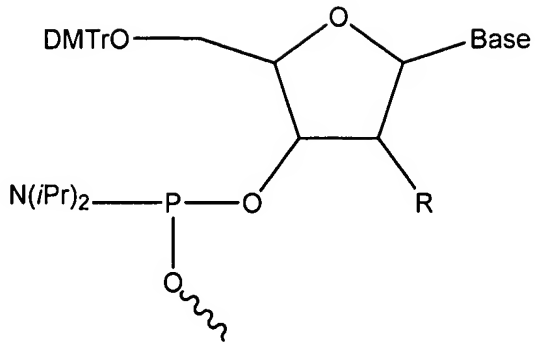
The rejection of claims 1-26 under 35 U.S.C. § 112, second paragraph, as being indefinite due to the use of the term "substituted," has been maintained. Claims 1, 2, 15 and 16 have been amended to recite that "said substituted moieties refer to molecules wherein one or more atoms of hydrogen have been replaced with a lower hydrocarbyl moiety or functional group selected from hydroxyl, alkoxy, thio, amino, and halo." In light of this amendment, applicant submits that the claims are definite in the sense that they particularly point out and distinctly claim the subject matter which applicant regards as the invention, and respectfully requests that the rejection be withdrawn.

Rejection under 35 U.S.C. § 102(a)

Claims 1-26 are rejected under 35 U.S.C. § 102(a) as being anticipated by Guzaev et al (US 6,121,437), the Examiner citing compounds with registry numbers 291299-97-3P, 291299-98-4P, 291300-40-8P, 291300-43-1P, 291300-46-4P, 291300-48-6P as meeting the structural limitations as set forth in the instant application. Applicant respectfully traverses the rejection for at least the following reasons.

The presently prosecuted claims are directed toward phosphonate or phosphino amidite derivatives with structures of formula III (see claims above). Compounds that are encompassed by formula III contain a phosphorus moiety directly attached to at least one carbon atom (i.e., either R^{11} or R^{12}). In contrast, the compounds cited by the Examiner and discussed in Guzaev contain a moiety with the structure of formula IIa:

(IIa)



wherein the wavy line represents an attachment point to the rest of the compound. The phosphorus moieties for each of the cited compounds contain three substituents, none of which allow for a carbon atom to be directly attached to the phosphorus atom as required by the claims of the current application. The claimed compounds are structurally distinct from those in Guzaev, and are therefore not anticipated by Guzaev. Accordingly, applicant respectfully requests removal of the rejection.

Rejection under 35 U.S.C. § 102(a)

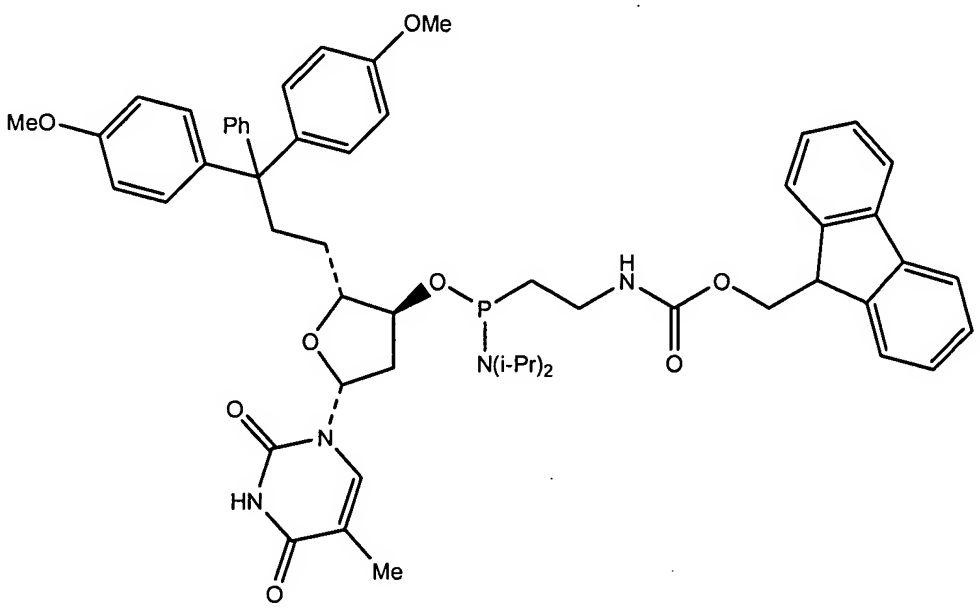
Claims 1-26 are rejected under 35 U.S.C. § 102(a) as being anticipated by Guzaev et al. ("A Novel Phosphate Protection for Oligonucleotide Synthesis: The 2-[(1-napthyl)carbamoyloxy]ethyl (NCE) Group" Tetrahedron Letters, vol. 41, 2000, pp 5623-5626), the Examiner citing compounds with registry numbers 291300-46-4P, 291300-48-6P, 295326-86-2P, and 295326-87-3P as meeting the structural limitations as set forth in the instant application. Applicant respectfully traverses the rejection for at least the following reasons.

As is the case for the compounds cited from US 6,121,437, the compounds cited by the Examiner and discussed in the Tetrahedron Letters reference to Guzaev ("Guzaev 2000") contain a moiety with the structure of formula IIa (see previous section). Similarly, the cited compounds do not contain a phosphorus moiety that is directly attached to a carbon atom, as required by the current claims. Accordingly, applicant submits that Guzaev 2000 does not anticipate the current claims, and respectfully requests removal of the rejection.

Rejection under 35 U.S.C. § 102(b)

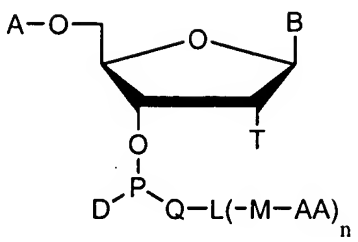
Claims 1-26 are rejected under 35 U.S.C. § 102(b) as being anticipated by Seliger et al (US 5,700,919), the Examiner citing the compound with registry number 134645-30-0P as meeting the structural limitations as set forth in the instant application. Applicant respectfully traverses the rejection for at least the following reasons.

The presently prosecuted claims are directed toward phosphonate or phosphino amidite derivatives with structures of formula III (see claims above). Compounds that are encompassed by formula III contain a phosphorus moiety directly attached to at least one carbon atom (i.e., either R^{11} or R^{12}). The cited compound, 5'-O-dimethoxytrityl-2'-deoxythymidine-3'-O-[2-(9-fluorenylmethoxycarbonyl)aminoethyl]-N,N-diisopropylamino-phosphane (CAS Registry No. 134645-30-0), is the title compound of Example 4 in Seliger, and is reported in the CAS registry as having the following structure:



However, applicant submits that the title of Example 4 in Seliger incorrectly names the structure that is actually intended. Seliger reports and claims phosphoramidite compounds, which have the general structure of formula (I)

(I)



wherein Q is oxygen or sulfur, D is a secondary amine residue, and the remaining substituents are defined in Seliger. Unlike the title compound of Example 4, structures that are encompassed by formula (I) are clearly limited such that the phosphorus atom can be directly connected only to heteroatoms (i.e., N, O or S). Therefore, the title compound of Example 4 is not encompassed by any of the structures in Seliger. Furthermore, Example 4 specifies two synthetic processes, both of which yield a phosphoramidite derivative wherein the phosphorus moiety is: (1) a P(III) derivative attached to the nucleoside through the 3'-hydroxyl; (2) bound to a nitrogen from a diisopropylamino group (i.e., D); and (3) substituted with an aminoethyl group protected by 9-fluorenylmethoxycarbonyl and bound to the phosphorus moiety through an oxygen atom (i.e., Q). Therefore, the compound that is actually produced by the synthetic processes of Example 4 has the structure of formula (I). No synthetic process for the preparation of the title compound of Example 4 can be found in Seliger. Furthermore, the CAS database lists only two references that cite 134645-30-0: a European patent application to Seliger, and Horn et al.[1] The European patent application to Seliger is in the same family as US 5,700,919, the reference cited by the Examiner, and is also directed toward phosphoramidites. Furthermore, the text of Horn does not identify any phosphonates or phosphino amidites, as required by the currently prosecuted claims. As is the case in Seliger, Horn et al. has synthetic procedures that are directed toward phosphoramidites (which do not contain a phosphorus moiety bonded directly to at least one carbon atom). Thus, it seems that no enabling disclosure of the synthesis of the title compound of Seliger's Example 4 is documented. Accordingly, applicants respectfully request the withdrawal of the rejection.

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[1] Horn et al. (1991), Nucleosides Nucleotides, 10(1-3), pp 299-302. See the Information Disclosure Statement that accompanies this amendment.

CONCLUSION

The above arguments and amendments are submitted in an effort to place this application in condition for allowance and for the purpose of facilitating allowance of the claims. A notice of allowance is earnestly requested.

If in the opinion of the Examiner, a telephone conference would clarify any remaining matters, or expedite the prosecution of the subject application, a telephone call to the undersigned at (650) 251-7724 would be appreciated.

Respectfully submitted,

By: 

Isaac Rutenberg
Registration No. 57,419

Reed Intellectual Property Law Group
1400 Page Mill Road
Palo Alto, California 94304
(650) 251-7700 Telephone
(650) 251-7739 Facsimile

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